

REMARKS

This is in response to the Office Action that was mailed on December 4, 2002. Claims 8, 10, and 11 are rewritten in independent form. New claims 15-18 are based upon original claims 1 and 5-7, respectively. The qualitative phrase "low flow velocity" throughout the claims is replaced by a quantitative phrase based upon such disclosure as that in the full paragraph on page 9 of the specification. No new matter is introduced by this Amendment. Entry of this Amendment, in order to place the application into condition for allowance or into better condition for appeal, is respectfully solicited. With this Amendment, claims 2, 8-13, and 15-18 are in the application.

FORMAL REJECTIONS. Claims 2 and 7-13 were rejected under the second paragraph of 35 U.S.C. § 112. The Examiner took the position that the metes and bound of "low flow velocity" cannot be determined. Applicants respectfully submit that the language "low flow velocity gradient high performance liquid chromatographic apparatus" is well known to those skilled in the art, as noted in the paragraph bridging pages 2-3 of the specification. Moreover, Applicants have in any case provided a detailed explanation of what that language means in the context of the present invention, in the full first paragraph on page 9 of the specification. However, in order to advance the prosecution of this application, the present Amendment replaces the qualitative language in question by a quantitative recitation. The Examiner also noted that in claim 9 the language "the component concentration column" lacked antecedent basis. The antecedence problem is resolved by the present Amendment. Applicants submit that the claims as amended herein satisfy the requirements of the statute. Accordingly, the Examiner is respectfully requested to withdraw this ground of rejection.

THE PRESENT INVENTION. The present invention distinguishes over the prior art of record by placing the diffusion promoting device just before the separation column. This permits a sample being analyzed to be retained uniformly at the beginning end of the separation column. The sample is diffused or dispersed uniformly by way of the diffusion promoting device before the separation column and it can be treated uniformly in the separation column. A sufficient concentration of the target compound in an eluent can thus be obtained to effect a gradient elution. "The present invention provides a diffusion promoting device provided just before a separation column and having a function of improving detection sensitivity, in a low flow velocity high performance liquid chromatographic apparatus. The present invention also provides a method for improving detection sensitivity of a target component for use in a low flow velocity gradient high performance liquid chromatographic apparatus, wherein a diffusion promoting device is provide just before a separation column." Specification, page 6, 2<sup>nd</sup> and 3<sup>rd</sup> full paragraphs. Thus -- in summary -- the presently claimed inventions are all characterized by placing a diffusion-promoting device (DU) just before a separation column (C) in a liquid stream line. This enables specimens to enter into the separation column with uniformity, thus providing chromatographic results with unexpectedly improved sensitivity.

KOCH. Claims 1, 2, and 5-8 were rejected under 35 U.S.C. §102(b) as being anticipated by, or in the alternative, under 35 U.S.C. §103(a) as being unpatentable over, US 4,475,821 (Koch). Claims 1 and 5-7 are cancelled. It is respectfully submitted that Koch neither teaches nor suggests that placing a diffusion-promoting device (DU) just before a separation column (C) in a liquid stream line enables specimens to enter into the separation column with uniformity, and thus provides chromatographic results with unexpectedly

improved sensitivity. Accordingly, it is respectfully requested that this ground of rejection be withdrawn.

ASAKAWA. Claims 1, 2, and 9-13 were rejected under 35 U.S.C. §102(b) as being anticipated by, or in the alternative, under 35 U.S.C. §103(a) as being unpatentable over, US 5,117,109 (Asakawa). Claims 12 and 13 were rejected under 35 U.S.C. §103(a) as being unpatentable over Asakawa in view of *Introduction to Modern Liquid Chromatography* (Snyder). Claim 1 is cancelled. It is respectfully submitted that Asakawa neither teaches nor suggests that placing a diffusion-promoting device (DU) just before a separation column (C) in a liquid stream line enables specimens to enter into the separation column with uniformity, and thus provides chromatographic results with unexpectedly improved sensitivity. It is additionally noted that in Asakawa, the pipe before TC is larger than the other pipe. Column 6, line 30. This means that the pipe 36 in Figure 1 is larger. The pipe 36 is followed by the trapping column (TC), the valve (V4), and the pipe 39 before arriving at the separation column (C3). This does not constitute "just before" as recited in the present claims. Accordingly, it is respectfully requested that this ground of rejection be withdrawn.

#### Conclusion

If the Examiner has any questions concerning this application, he is requested to contact Richard Gallagher, Reg. No. 28,781, at (703) 205-8000 in the Washington, D.C. area.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of one (1) month to April 4, 2003, in

which to file a reply to the Office Action. The required fee of \$110.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By *Marc S. Weiner*  
Marc S. Weiner  
Reg. No. 32,181

P. O. Box 747  
Falls Church, VA 22040-0747  
(703) 205-8000

MSW/RG *RG*

Attachment: Version with Markings to Show Changes Made

***Marked up text showing changes:***

Claims 1 and 5-7 have been canceled.

The claims have been amended as follows:

2. (twice amended) A method for improving a detection sensitivity of a target component, which comprises providing the diffusion promoting device just before a separation column in a [low flow velocity gradient] high performance liquid chromatographic apparatus having a flow velocity gradient of 250 microliters per minute or less, wherein said diffusion promoting device comprises a solvent inlet tube and a solvent outlet tube and wherein said device includes at least one feature selected from the group consisting of (i) having a solvent inlet tube and a solvent outlet tube with different inner diameters, (ii) having a solvent outlet tube connected to a solvent inlet tube at an acute angle, a right angle, or an obtuse angle, and (iii) having a solvent outlet tube connected to a solvent inlet tube by a connecting part having a diameter that is larger than the diameters of the diameters of the solvent inlet and outlet tubes.

8. (twice amended) A [low flow velocity gradient] high performance liquid chromatographic apparatus having a flow velocity gradient of 250 microliters per minute or less, said apparatus comprising [the] a diffusion promoting device that comprises a solvent inlet tube and a solvent outlet tube, wherein said device includes at least one feature selected from the group consisting of (i) having a solvent inlet tube and a solvent outlet tube with different inner diameters, (ii) having a solvent outlet tube connected to a solvent inlet tube at

an acute angle, a right angle, or an obtuse angle, and (iii) having a solvent outlet tube connected to a solvent inlet tube by a connecting part having a diameter that is larger than the diameters of the diameters of the solvent inlet and outlet tubes, said diffusion promoting device being positioned [according to Claim 1 at] just before the separation column.

9. (twice amended) The [A low flow velocity] high performance liquid chromatographic apparatus according to claim 8, in which the diffusion promoting device [according to Claim 1] is connected between [the] a component concentration column and the separation column.

10. (thrice amended) A [low flow velocity gradient] high performance liquid chromatographic apparatus having a flow velocity gradient of 250 microliters per minute or less, said apparatus in which a solvent pump (P1), an injector (I), and a switching valve (V) are connected in this order in one line; and a solvent pump (P2), a switching valve (V), [the] a diffusion promoting device (DU) [according to Claim 1,] that comprises a solvent inlet tube and a solvent outlet tube, wherein said device includes at least one feature selected from the group consisting of (i) having a solvent inlet tube and a solvent outlet tube with different inner diameters, (ii) having a solvent outlet tube connected to a solvent inlet tube at an acute angle, a right angle, or an obtuse angle, and (iii) having a solvent outlet tube connected to a solvent inlet tube by a connecting part having a diameter that is larger than the diameters of the diameters of the solvent inlet and outlet tubes, a separation column (C), and a detector (D) are connected in another line.

11. (thrice amended) A [low flow velocity gradient] high performance liquid chromatographic apparatus having a flow velocity gradient of 250

microliters per minute or less, said apparatus in which a solvent pump (P1), a switching valve (V), a solvent mixer (MC), and a switching valve (V) are connected in this order in one line; a solvent pump (P2), a switching valve (V), [the] a diffusion promoting device (DU) [according to Claim 1,] that comprises a solvent inlet tube and a solvent outlet tube, wherein said device includes at least one feature selected from the group consisting of (i) having a solvent inlet tube and a solvent outlet tube with different inner diameters, (ii) having a solvent outlet tube connected to a solvent inlet tube at an acute angle, a right angle, or an obtuse angle, and (iii) having a solvent outlet tube connected to a solvent inlet tube by a connecting part having a diameter that is larger than the diameters of the diameters of the solvent inlet and outlet tubes, a separation column (C), and a detector (D) are connected in another line; and a switching valve (V), a component concentration column (M), and a switching valve (V) are connected in a different line.

12. (twice amended) A method for analyzing a trace amount of a component in a sample with improved detection sensitivity for use in the [low flow velocity gradient] high performance liquid chromatographic apparatus according to Claim 10, which comprises trapping the target component in the component concentration column (M) by means of a mobile phase discharged from the solvent pump (P1); discharging a different mobile phase from the solvent pump (P2) by turning the switching valve; and eluting the target component from the separation column (C) through diffusion of the target component using the diffusion promoting device (DU).

13. (twice amended) A method for analyzing a trace amount of a component in a sample with improved detection sensitivity for use in the [low flow velocity gradient] high performance liquid chromatographic apparatus

according to Claim 11, which comprises injecting the target component into the component concentration column (M) while filling a solvent in the solvent mixer (MC) by means of the solvent pump (P1); discharging a mobile phase from the pump (P2) by turning the switching valve; and eluting the target component from the separation column (C) through diffusion of the target component using the diffusion promoting device (DU).

Claims 15-18 have been added.